

Patent claims

1. Method of producing a self-hardening bioabsorbable composite material, wherein
 - (i) a polymerisation initiator is immobilised with the aid of a first partial amount of an interconnectingly porous bioabsorbable inorganic bone regeneration material,
 - (ii) a polymerisation activator is immobilised with the aid of a second partial amount of the bone regeneration material according to (i) or of a different interconnectingly porous bioabsorbable inorganic bone regeneration material,
 - (iii) the components obtained in steps (i) and (ii) are mixed with a liquid or paste-form multi-functional monomer capable of polymerisation to form a biocompatible and bioabsorbable polymer or with a liquid or paste-form mixture of multi-functional monomers capable of polymerisation to form a biocompatible and bioabsorbable polymer, and
 - (iv) the monomer or monomer mixture contained in the mixture produced is polymerised and the composite material is obtained.
2. Method according to claim 1, wherein, especially in step (iii), constituents which modify the properties of the monomer, monomer mixture and/or composite material are mixed in.
3. Method according to claim 2, wherein one or more modifying constituents are mixed in which are selected from the group: thickeners, diluents, polymeric fillers, porogens, pH-modifying substances, colourants and adhesion-imparting agents.
4. Method according to at least one of the preceding claims, characterised in that at least one of the constituents mixed in is a substance which alters the viscosity of the monomer, the monomer mixture and/or the mixture thereof with the bone regeneration material.
5. Method according to claim 4, characterised in that the substances altering the viscosity of the monomer, the monomer mixture and/or the mixture thereof with the bone regeneration material are oligomeric or polymeric derivatives of alpha-hydroxycarboxylic acids, preferably those of lactic and/or glycolic acid, and/or are substances from the group of oligo- and poly-ethylene glycols.
6. Method according to claim 4 and/or 5, characterised in that dianhydro-D-glucitol-bis(poly-D,L-lactide) is used as viscosity-increasing substance.

7. Method according to at least one of the preceding claims, characterised in that at least one of the constituents mixed in is a substance which is water-soluble or which reacts with water to form water-soluble resultant products and which brings about a pH change in a water-containing medium.

8. Method according to at least one of the preceding claims, characterised in that at least one of the constituents mixed in is a water-soluble pore-forming substance which is added to the monomer, monomer mixture and/or the mixture thereof with the bone regeneration material in particulate form.

9. Method according to claim 7 and/or 8, characterised in that sodium hydrogen carbonate is used as water-soluble pH-modifying and pore-forming substance.

10. Method according to at least one of the present claims, characterised in that at least one of the constituents mixed in is a substance which acts as an adhesion-imparting agent between the composite material and living tissue, preferably hard tissue.

11. Method according to claim 10, characterised in that hydroxyl-group-containing adhesion-imparting agents, preferably methacrylic acid 2-hydroxyethyl ester, are used as adhesion-imparting agent.

12. Method according to at least one of the present claims, characterised in that at least one of the constituents mixed in is a colourant or a contrast agent.

13. Method according to at least one of the preceding claims, characterised in that at least one of the constituents mixed in is a pharmaceutical active ingredient or an active ingredient mixture for local therapy and/or prophylaxis.

14. Method according to claim 13, characterised in that antibiotics, anti-inflammatories, proteinogenic growth factors and/or cancerostatics are used as pharmaceutical active ingredients.

15. Method according to at least one of the preceding claims, wherein the first partial amount and the second partial amount of the bone regeneration material are used in a

ratio of from 1:10 to 10:1 and/or the polymerisation initiator and the polymerisation activator are immobilised with the respective partial amounts of the bone regeneration material in a ratio of from 1:10 to 10:1 (based on weight in each case).

16. Method according to at least one of the preceding claims, wherein the bone regeneration material is used in the form of powder or granules.

17. Method according to at least one of the preceding claims, wherein, in step (i) according to claim 1, a solution of the polymerisation initiator is added to the bone regeneration material, the solution is allowed to infiltrate the bone regeneration material, and afterwards the bone regeneration material is dried.

18. Method according to at least one of the preceding claims, wherein a solution of the polymerisation initiator is mixed with the bone regeneration material in an amount of from 0.1 to 20 % by weight (solid initiator based on bone regeneration material).

19. Method according to at least one of the preceding claims, wherein an organic peroxide is used as polymerisation initiator, preferably an organic peroxide selected from the group comprising dibenzoyl peroxide, lauroyl peroxide and acetone peroxide.

20. Method according to at least one of the preceding claims, wherein, in step (ii) according to claim 1, a melt or solution of the polymerisation activator is added to the bone regeneration material, the solution is allowed to infiltrate the bone regeneration material, and afterwards the bone regeneration material is dried.

21. Method according to at least one of the preceding claims, wherein a solution of the polymerisation activator is mixed with the bone regeneration material in an amount of from 0.1 to 20 % by weight (solid activator based on bone regeneration material).

22. Method according to at least one of the preceding claims, wherein one or more polymerisation activators are used which are selected from the group comprising N,N-bis(2-hydroxyethyl)-p-toluidine, N,N-dimethyl-p-toluidine, N,N-dimethyl-N,N-aniline, ascorbic acid and barbituric acid.

23. Method according to at least one of the preceding claims, wherein the polymerisation initiator is used in the form of a solution and/or the polymerisation activator is used in the form of a solution and the solution(s) is/are allowed to be drawn up by the bone regeneration material completely or as far as possible and the excess not drawn up is removed before step (iii) according to claim 1.

24. Method according to at least one of the preceding claims, wherein there is used, as inorganic bone regeneration material, an alkaline earth metal phosphate and/or an alkali metal/alkaline earth metal phosphate, especially an alkaline earth metal orthophosphate and/or alkali metal/alkaline earth metal orthophosphate, preferably a bone regeneration material which is selected from the group comprising alpha-tricalcium phosphate, beta-tricalcium phosphate, calcium-deficient carbonate-containing hydroxyapatite, octacalcium phosphate, magnesium phosphate, calcium hydrogen phosphate, calcium/sodium orthophosphate and calcium pyrophosphate.

25. Method according to at least one of the preceding claims, wherein the same bone regeneration material is used for the immobilisation of the polymerisation initiator as for the immobilisation of the polymerisation activator.

26. Method according to claim 25, wherein the bone regeneration material for the immobilisation of the initiator and the bone regeneration material for the immobilisation of the activator differ from one another in their chemical and/or mineralogical nature.

27. Method according to at least one of the preceding claims, wherein an interconnectingly porous bone regeneration material, especially calcium phosphate, having the following characteristic data is used:

- pore diameters from 0.1 to 500 μm , preferably from 0.1 to 100 μm and especially from 0.1 to 100 μm , and/or
- particle sizes (d_{50} values) of from 1 to 500 μm , preferably from 5 to 300 μm , and/or
- BET surface area of at least 0.1 m^2/g .

28. Method according to at least one of claims 1 to 26, wherein there is used an interconnectingly porous bone regeneration material, especially calcium phosphate, having a pore volume, accessible to the polymerisation initiator and/or the polymerisation

activator, of $0.4 \text{ cm}^3/\text{g}$ or more, and especially from 0.4 to $3.3 \text{ cm}^3/\text{g}$, while retaining the integrity of the particles of the bone regeneration material.

29. Method according to at least one of the preceding claims, wherein the bone regeneration material, especially calcium phosphate, is used in crystalline, partly crystalline, glassy or amorphous form.

30. Method according to at least one of the preceding claims, especially according to claim 2 and/or 3, wherein constituents which are biocompatible and which modify the properties of the regeneration material, especially silicon compounds, are mixed in with the bone regeneration material.

31. Method according to at least one of the preceding claims, wherein there is used, as the monomer or as monomers of the monomer mixture, a multi-functional oligomer having terminal methacrylate groups, especially an oligomer of lactic acid and/or glycolic acid and/or delta-hydroxyvaleric acid and/or epsilon-hydroxycaproic acid and/or trimethylene carbonate.

32. Self-hardened bioabsorbable composite material which can be produced by

- (i) immobilising a polymerisation initiator with the aid of a first partial amount of the bone regeneration material according to (i) or a different interconnectingly porous bioabsorbable inorganic bone regeneration material,
- (ii) immobilising a polymerisation activator with the aid of a second partial amount of the bone regeneration material according to (i) or of a different interconnectingly porous bioabsorbable inorganic bone regeneration material,
- (iii) mixing the components obtained in steps (i) and (ii) with a liquid or paste-form multi-functional monomer capable of polymerisation to form a biocompatible and bioabsorbable polymer or with a liquid or paste-form mixture of multi-functional monomers capable of polymerisation to form a biocompatible and bioabsorbable polymer, and
- (iv) polymerising the monomer or monomer mixture contained in the mixture produced and obtaining the composite material.

33. Composite material according to claim 32, having a weight ratio of bone regeneration material : monomer or monomer mixture of from 4 : 6 to 8 : 2.

34. Composite material according to claim 32 and/or 33, obtainable by a method according to at least one of claims 2 to 31.

35. Self-hardening bioabsorbable composite material in the form of a set, consisting of or comprising

- (i) a first partial amount of an interconnectingly porous bioabsorbable inorganic bone regeneration material and a polymerisation initiator which is immobilised with the aid of that first partial amount,
- (ii) a second partial amount of the bone regeneration material according to (i) or of a different interconnectingly porous bioabsorbable inorganic bone regeneration material and a polymerisation activator which is immobilised with the aid of that second partial amount, and
- (iii) a liquid or paste-form multi-functional monomer capable of polymerisation to form a biocompatible and bioabsorbable polymer or a liquid or paste-form mixture of multi-functional monomers capable of polymerisation to form a biocompatible and bioabsorbable polymer.

36. Composite material according to claim 35, having a weight ratio of bone regeneration material : monomer or monomer mixture of from 4 : 6 to 7 : 3.

37. Composite material in the form of a set according to claim 35 and/or 36, wherein the components (i), (ii) and (iii) are obtainable by a method according to at least one of claims 2 to 31.

38. Use of a self-hardened composite material according to at least one of claims 32 to 34 in machine-production of implants in the form of shaped pieces of standardised dimensions for bone regeneration or of implants that are individual to a patient.

39. Use of a self-hardening bone regeneration material in the form of a set according to at least one of claims 35 to 37 in producing a bone adhesive for the fixing of bone fractures.